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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,889	11/28/2000	Bryan Julien	300622003111	7394
7590 03/23/2004				
RANDOLPH TED APPLE MORRISON & FOERSTER LLP 755 PAGE MILL ROAD PALO ALTO, CA 94304-1018		EXAMINER NASHED, NASHAAT T		
		ART UNIT PAPER NUMBER 1652		

DATE MAILED: 03/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/724,889

Applicant(s)

JULIEN ET AL.

Examiner

Nashaat T. Nashed, Ph. D.

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--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 11 March 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:


Claim(s) allowed: \_\_\_\_\_

Claim(s) objected to: \_\_\_\_\_

Claim(s) rejected: 15-17, and 25, 29-34.

Claim(s) withdrawn from consideration: \_\_\_\_\_

8. ☒ The drawing correction filed on \_\_\_\_\_ is a) ☒ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_



Nashaat T. Nashed, Ph. D.  
Primary Examiner  
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Claims 15-17, 25, and 29-34 are under consideration.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 15-17, 25 and 29-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schupp *et al.* (Schupp, IDS paper number 13, Ref.No. 5, U. S. Patent 6,355,459) in view Khosla *et al.* (Khosla A, IDS reference, paper number 10, reference number 10, U. S. Patent 6,391,594), and Khosla *et al.* (Khosla B, IDS paper number 11, Ref No. 33: WO 97/02358).

In response to the above rejections, Applicants amended claims 15 and 29 to indicate that the epothilone derivative with a double bond between C-12 and C-13, and continue to argue the chemical structure of the resulting derivative of epothilone D.

Applicants' arguments filed 3/11/04 have been fully considered but they are not deemed to be persuasive. The claimed invention is directed to a modified *epoE* gene product, which is a polyketide synthase. The claims are not directed to a method of making any chemical compound having any particular chemical structure. Thus, all applicants' argument regarding the chemical structure of a product made by the modified *epoE* has no relevance to these rejections. The main questions that are relevant to the obviousness rejection of the claimed modified *epoE* are: (a) was the *epoE* gene from *Sorangium cellulosum* known in the prior art at the time of invention? (b) was there a motivation to one of ordinary skill in the art to make the claimed *epoE* polyketide synthase? and, (c) would an ordinary skill in the art have expected to succeed in making the modification and obtaining the protein? The answers to all three questions are yes. The cited prior art of Schupp *et al.* taught the entire gene cluster and its products, which are required for the biosynthesis of epothilones. Khosla A and Khosla B provide the motivation and expectation of success. Once the ordinary skill in the art, he/she would have been further motivated to combine all or some of the protein products, which are required for the biosynthesis of epothilone to make variety of analogs of epothilones and their precursors. While applicants intended reason(s) to obtain a modified *epoE* may have been different, i. e., produces an epothilone D derivative with double bond between C-12 and C-13, from that one of ordinary skill in the, the rejections remain valid because would have made the same protein to make

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various derivatives of epothilone A and B, as well as D. Epothilone D is a precursor to both epothilone A and B. Claims 16 and 17 are not limited to an epothilone D derivatives because the system comprised other enzymes to modify the polyketide product such as epoxidation or addition reactions of the double. Thus, the claims remain rejected for the reasons of record.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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